COMPARATIVE STUDY OF CHEST X – RAY FEATURES IN PULMONARY TUBERCULOSIS WITH AND WITHOUT HIV CO-INFECTION

DISSERTATION SUBMITTED FOR

DOCTOR OF MEDICINE

BRANCH - I (GENERAL MEDICINE)

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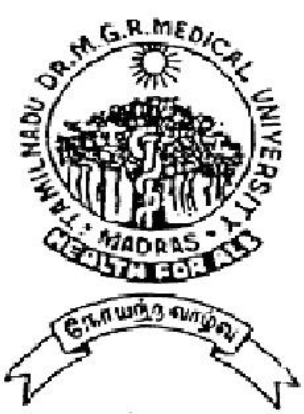

THE TAMILNADU
DR.M.G.R.MEDICAL UNIVERSITY
CHENNAI

BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF CHEST X – RAY FEATURES IN PULMONARY TUBERCULOSIS WITH AND WITHOUT HIV CO-INFECTION"** submitted by **Dr. N. TAHSIN** to the Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.D Degree Branch –I (General Medicine) is a bonafide research work were carried out by him under my direct supervision & guidance.

Prof.Dr.V.T.Premkumar, M.D.,
Unit Chief,
Department of Medicine,
Madurai Medical College,
Madurai.

Prof.Dr.A.Ayyappan, M.D.,
Head of the Department,
Department of Medicine,
Madurai Medical College,
Madurai.

DECLARATION

I **Dr. N. TAHSIN** declare that, I carried out this work on, **"A COMPARATIVE STUDY OF CHEST X – RAY FEATURES IN PULMONARY TUBERCULOSIS WITH AND WITHOUT HIV CO-INFECTION"** at the Department of Medicine, Govt. Rajaji Hospital during the period of March 2008 to August 2008. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, diploma to any other University, Board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D degree examination in General Medicine.

Place : Madurai **Dr. N. TAHSIN**

Date :

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CONTENTS

INTRODUCTION

Tuberculosis is a specific infectious disease caused by mycobacterium tuberculosis. The disease primarily affects lungs and causes pulmonary tuberculosis.

Tuberculosis remains a world wide public health problem despite the fact that the causative organism was discovered more than 100 years ago. It is estimated that about 1/3 rd of current global population is infected asymptomatically with tuberculosis of whom 5-10 percent will develop clinical disease during their life time. Most new cases and deaths occur in developing countries where infection is often acquired in childhood. Comparing different parts of the world the African region (24%). South east Asia region (35%) and Western Pacific region (24%) together accounted for 83% of all notified new and relapse cases.[3]

India is the highest TB burden country in the world and accounts for nearly one fifth (20%) of global burden of tuberculosis. Every year approximately 1.8 million persons

develop tuberculosis of which about 0.8 million are new smear positive highly infectious cases.

World wide the number of people infected with both HIV and tuberculosis is rising. The HIV virus damages the body natural defenses – the immune system – and accelerates the speed at which TB progresses from a harmless infection to a life threatening condition. TB has already become the most frequent opportunistic infection that kills HIV positive people. The diagnosis of tuberculosis in individual patients using the standard diagnostic tools can be more difficult if they have advanced HIV infection.

HIV and tuberculosis interact in several ways

1. Reactivation of latent infection : People who are infected with both tuberculosis and HIV are 25-30 times more likely to develop tuberculosis. This is because HIV stops the immune system working effectively and tuberculosis bacilli are able to multiply rapidly. In developing

countries HIV associated tubercular disease is very common.

2. Primary infection : New tubercular infection in people with HIV can progress to active disease very quickly. In the USA active tubercular disease in two thirds of people with both infections is due to recent infection rather than reactivation of latent infection. People with HIV are at risk of being newly infected, if they are exposed to tuberculosis because their weakened immune system makes them more vulnerable.

3. Recurring Infection : People with HV who have been cured of tuberculosis infection may be more at risk of developing tuberculosis again. However it is not clear whether this is because of reinfection or relapse.

4. In the community : There are more new cases of active tuberculosis because more people infected with tuberculosis develop active disease, and those newly infected become ill faster. This means that there are more people in the community who are infectious to others. Larger number of people with active disease mean more people will die from tuberculosis unless they are treated. The association of tuberculosis with HIV means that people suffer additional discrimination. Community education is needed to increase awareness that tuberculosis is curable and most important, that people are no longer infectious after the first few weeks of treatment.

In most people in the early stages of HIV infection, symptoms of tuberculosis are similar as in people without HIV infection. In areas where many people have HIV infection, tuberculosis programmes should continue to focus on identifying infectious sputum-smear-positive cases through

microscopy. However, diagnosis of tuberculosis in individual patients using the standard diagnostic tools can be more difficult if they have advanced HIV infection because :

a) HIV positive people with pulmonary tuberculosis may have a higher frequency of negative sputum smears. Confirming the diagnosis may require sputum culture.

b) The tuberculosis skin test often fails to work in people who are HIV positive because it relies on measuring the response of a person's immune system. If the immune system has been damaged by HIV, it may not respond even though the person is infected with tuberculosis. HIV positive people with tuberculosis, therefore have a higher frequency of false negative tuberculin skin test results.

c) Cases of extra pulmonary tuberculosis seem to be more common in people who are co-infected.

d) Chest radiography may be less useful in people with HIV because they have less cavitation. Cavities usually develp because the immune response to the tubercular bacilli leads to some destruction of lung tissue. In people with HIV, who do not have a fully functioning immune system, there is less tissue destruction and hence less lung cavitation.

The radiological manifestations of tuberculosis in HIV infected patients may vary according to the degree of immuno suppression.

AIM OF THE STUDY

- To compare the chest X ray features of HIV positive pulmonary tuberculosis patients with HIV negative pulmonary tuberculosis patients.
- To determine the percentage of patients with atypical chest x ray in HIV positive and negative groups
- To determine the relationship between atypical chest x rays and CD4 count.

REVIEW OF LITERATURE

Tuberculosis:

Tuberculosis, one of the oldest diseases known to affect humans, is a major cause of death worldwide. If properly treated, tuberculosis caused by drug-susceptible strains is curable in virtually all case. If untreated, the disease may be fatal within 5 years in 50-65% of cases. Transmission usually takes place through the airborne spread of droplet nuclei produced by patients with infectious pulmonary tuberculosis. Mycobacteria belong to the family Mycobacteriaceae and the order actinomycetales.

M.Tuberculosis is a rod-shaped, non-spore-forming, thin aerobic bacterium measuring 0.5μm by 3μm. Mycobacteria, including M.tuberculosis, are often neutral on Gram's staining. However, once stained, the bacilli cannot be decolorized by acid alcohol; this characteristic justifies their classification as acid-fast bacilli. Acid fastness is due mainly to the organisms' high content

of mycolic acids, long-chain cross-linked fatty acids, and other cell-wall lipids.

More than 5 million new cases of tuberculosis (all forms, both pulmonary and extrapulmonary) were reported to the World Health Organization (WHO) in 2005;>90% of cases were reported from developing countries. [1]

Recent data on trends indicate that in 2005 tuberculosis incidence was stable or falling in most regions; the result is a small decline globally from figures in previous years. This global reduction is due largely to an apparent peaking in sub-Saharan Africa, where incidence had risen steeply since the 1980s as a result of the HIV epidemic and the paucity of the health services. In eastern Europe, incidence increased during the 1990s because of deterioration in socioeconomic conditions and the health care infrastructure; however, after peaking in 2001, incidence has recently stabilized.

From exposure to infection:-

M.Tuberculosis is most commonly transmitted from a person with infectious pulmonary tuberculosis to others by droplet nuclei, which are aerosolized by coughing, sneezing, or speaking. There may be as many as 3000 infectious nuclei per cough. [1]

The most infectious patients have cavitary pulmonary disease or much less commonly, laryngeal tuberculosis and produce sputum containing as many as 10^5-10^7 AFB/mL. Patients with sputum smear-negative/culture-positive tuberculosis are less infectious, and those with culture-negative pulmonary disease and extrapulmonary tuberculosis are essentially noninfectious. Because persons with both HIV infection and tuberculosis are less likely to have cavitations, they may be less infectious than persons without HIV co-infection.

From infection to disease:-

Unlike the risk of acquiring infection with M.Tuberculosis, the risk of developing disease after being infected depends

largely on endogenous factors, such as the individual's innate immunologic and nonimmunologic defenses and level of function of cell mediated immunity (CMI). Clinical illness directly following infection is classified as primary tuberculosis and is common among children up to 4 years of age and among immunocompromised persons. Although primary tuberculosis may be severe and disseminated , it is not generally associated with high-level transmissibility. When infection is a acquired later in life, the chance is greater that the mature immune system will contain it at least temporarily. The majority of infected individuals who ultimately develop tuberculosis do so within the first year or two after infection. Dormant bacilli, however, may persist for years before reactivating to produce secondary (or postprimary) tuberculosis, which, because of frequent cavitation, is more often infectious than is primary disease. Overall, it is estimated that upto 10% of infected persons will eventually develop active tuberculosis in their lifetime. The risk is much higher among HIV-infected persons. Among infected persons, the

incidence of tuberculosis is highest during late adolescene and early adulthood; the reasons are unclear.

Natural history of disease:-

Studies conducted in various countries before the advent of chemotherapy showed that untreated tuberculosis is often fatal. About one-third of patients died within 1 year after diagnosis, and one-half died within 5 years. The 5 year mortality rate among sputum smear-positive cases was 65%. Of the survivors at 5 years, ~60% had undergone spontaneous remission, while the remainder were still excreting tubercle bacilli. [1,3]

Clinical Manifestations:-

Tuberculosis is classified as pulmonary, extrapulmonary, or both. Before the advent of HIV infection, ~80% of all new cases of tuberculosis were limited to the lungs.However, upto two-thirds of HIV-infected patients with tuberculosis may have both pulmonary and extrapulmonary disease or extrapulmonary disease alone.

Primary disease:-

Primary pulmonary tuberculosis occurs soon after the initial infection with tubercle bacilli. In areas of high tuberculosis transmission, this form of disease is often seen in children. Because most inspired air is distributed to the middle and lower lung zones, these areas of the lungs are most commonly involved in primary tuberculosis. The lesion forming after infection is usually peripheral and accompanied in more than half of cases by hilar or paratracheal lymphadenopathy, which may not be detectable on chest radiography. In the majority of cases, the lesion heals spontaneously and may later be evident as a small calcified nodule. (Ghon lesion)

Postprimary disease:-

Also called adult-type, reactivation, or secondary tuberculosis, postprimary disease results from endogenous reactivation of latent infection and is usually localized to the apical and posterior segments of the upper lobes, where the substantially higher mean oxygen tension (compared with that in

the lower zones) favours mycobacterial growth, In addition, the superior segments of the lower lobes are frequently involved. The extent of lung parenchymal involvement varies greatly, from small infiltrates to extensive cavitary disease. With cavity formation, liquefied necrotic contents are ultimately discharged into the airways, resulting in satellite lesions within the lungs that may in turn undergo cavitation. Massive involvement of pulmonary segments or lobes, with coalescence of lesions, produces tuberculous pneumonia. While up to one-third of untreated patients reportedly succumb to severe pulmonary tuberculosis within a few weeks or months after onset (the classical “galloping consumption” of the past), others undergo a process of spontaneous remission or proceed along a chronic, progressively debilitating course (“consumption”). Under these circumstances, some pulmonary lesions become fibrotic and may later calcify, but cavities persist in other parts of the lungs.

Early in the course of disease, symptoms and signs are often non-specific and insidious, consisting mainly of fever and night

sweats, weight loss, anorexia, general malaise, and weakness. However in the majority of cases, cough eventually develops- often initially nonproductive and subsequently accompanied by the production of purulent sputum, sometimes with blood streaking.

Physical findings are of limited use in pulmonary tuberculosis. Many patients have no abnormalities detectable by chest examination, whereas others have detectable rales in the involved areas during inspiration, especially after coughing. Occasionally, rhonchi due to partial bronchial obstruction and classic amphoric breath sounds in areas with large cavities may be heard. Systemic features include fever (often low-grade and intermittent) in up to 80% of cases and wasting.

Extrapulmonary tuberculosis:-

In order of frequency, the extrapulmonary sites most commonly involved in tuberculosis are the lymph nodes, pleura, genitourinary tract, bones and joints, meninges, peritoneum, and pericardium. However, virtually all organ systems may be

affected. As a result of hematogenous dissemination in HIV-infected individuals, extrapulmonary tuberculosis is seen more commonly today than in the past.

Diagnosis of tuberculosis:-

The key to the diagnosis of tuberculosis is a high index of suspicion.

AFB Microscopy:-

A presumptive diagnosis is commonly based on the findings of AFB on microscopic examination of a diagnostic specimen, such as a smear of expectorated sputum or of tissue (e.g., a lymph node biopsy). Although rapid and inexpensive, AFB microscopy has relatively low sensitivity (40-60%) in confirmed cases of pulmonary tuberculosis. Most modern laboratories processing large numbers of diagnostic specimens use auramine-rhodamine staining and fluorescence microscopy. The more traditional method- light microscopy of specimens stained with Kinyoun or Ziehl-Neelsen basic fuchsin dyes-is satisfactory, although more time-consuming. For patients with suspected

pulmonary tuberculosis, three sputum specimens, preferably collected early in the morning should be submitted to the laboratory for AFB smear and mycobacterial culture.

Mycobacterial Culture:-

Definitive diagnosis depends on the isolation and identification of M.Tuberculosis from a clinical specimen or the identification of specific sequences of DNA in a nucleic acid amplification test (see below). Specimens may be inoculated onto egg- or agar- based medium (e.g., Lowenstein-Jensen or Middlebrook 7H10) and incubated at 37^{o}c (under 5% CO_2 for Middlebrook Medium). Because most species of mycobacteria, including M.Tuberculosis, grow slowly, 4-8 weeks may be required before growth is detected.

Nucleic Acid Amplification:-

Several test systems based on amplification of mycobacterial nucleic acid are available. These systems permit the diagnosis of tuberculosis in as little as several hours, with high specificity and sensitivity approaching that of culture.

Radiographic procedures:-

The initial suspicion of pulmonary tuberculosis is often based on abnormal chest radiographic findings in a patient with respiratory symptoms. Although the “classic” picture is that of upperlobe disease with infiltrates and cavities virtually any radiographic pattern-from a normal film or a solitary pulmonary nodule to diffuse alveolar infiltrates in a patient with ARDS-may be seen. In the era of AIDS, no radiographic pattern can be considered pathognomonic. CT may be useful in interpreting questionable findings on plain chest radiography and may be helpful in diagnosing some forms of extrapulmonary tuberculosis e.g., Pott’s disease. MRI is useful in the diagnosis of intracranial tuberculosis.

Serologic and other diagnostic tests for active tuberculosis:-

Determination of ADA levels in pleural fluid may be useful in the diagnosis of pleural tubercolusis; the utility of this test in the diagnosis of other forms of extrapulmonary tuberculosis (e.g. pericardial, peritoneal, and meningeal) is less clear.

Tuberculosis skin testing:-

In 1891, Robert Koch discovered that components of M.Tuberculosis in a concentrated liquid culture medium, subsequently named “old tuberculin” (OT),were capable of eliciting a skin reaction when injected subcutaneously into patients with tuberculosis. In 1932, Seibert and Munday purified this product by ammonium sulfate precipitation to produce an active protein fraction known as tuberculin purified Glenn, was chosen as the international standard. Later, the WHO and UNICEF sponsored large scale production of a master batch of PPD (RT23) and made it available for general use. The greatest limitation of PD is its lack of mycobacterial species specificity, a property due to the large number of proteins in this product that

are highly conserved in the various species. In addition, subjectivity of the skin-reaction interpretation deterioration of the product, and batch-to-batch variations limit the usefulness of PPD.

Skin testing with tubercuilin-PPD (TST) is most widely used in screening for latent M.Tuberculosis infection (LTBI). The test is of limited value in the diagnosis of active tuberculosis because of its relative of low sensitivity and specificity and its inability to discriminate between latent infection and active disease.

IFN - Gamma Release Assays (IGRAs):-

Recently, two in vitro assays that measure T cell release of IFN-gamma in response to stimulation with the highly tuberculosis specific antigents ESAT-6 and CFP-10 have become commercially available. Quanti FERON-TB Gold® (cellestis Ltd., Carnegie, Australia) is a whole blood enzyme-linked immunosorbent assay (ELISA) for measurement of IFN-y and T-SPOT.TB ® (Oxford Immunotec, Oxford, UK) is an enzyme-

linked immunospot (ELISpot) assay. IGRAs are more specific than the TST as a result of less Cross-reactivity due to BCG vaccination and sensitization by nontuberculous mycobacteria. IGRAs also appear to be at least as sensitive as the TST in active tuberculosis. [1]

Because of the high specificity and other potential advantages, IGRAs are likely to replace the TST for LTBI diagnosis in low-incidence, high-income settings where cross-reactivity due to BCG might adversely impact the interpretation and utility of the TST.

Treatment of Tuberculosis:-

The two aims of tuberculosis treatment are to interrupt tuberculosis transmission by rendering patients noninfectious and to prevent morbidity and death by curing patients with tuberculosis.

Drugs:-

Four major drugs are, considered the first-line agents for the treatment of tuberculosis:isoniazid, rifampin, pyrazinamide, and ethambutol

Because of a lower degree of efficacy and a higher degree of intolerability and toxicity, six classes of second-line drugs are generally used only for the treatment of patients with tuberculosis resistant to first line drugs. Included in this group are the injectable aminoglycosides streptomycin (formerly a first line agent), kanamycin, and amikacin; the injectable polypeptide capreomycin; the oral agents ethionamide, cycloserine, and PAS; and the fluoroquinolone antibiotics. Of the quinolones, third generation agents are preferred; levofloxacin, gatifloxacin and moxifloxacin.

HIV-ASSOCIATED TUBERCULOSIS

Tuberculosis is one of the most common diseases among HIV-infected persons worldwide. In some African countries, the rate of HIV infection among tuberculosis patients reaches 70-80% in certain urban settings. A person with a positive TST who acquires HIV infection has a 3-13% annual risk of developing active tuberculosis. A new tuberculosis infection acquired by an HIV –infected individual may evolve to active disease in a matter of weeks rather than months or years. [1,2]

Tuberculosis can appear at any stage of HIV infection, and its presentation varies with the stage. When CMI is only partially compromised, pulmonary tuberculosis presents in a typical manner, with upper-lope infiltrates and cavitation and with out significant lymphadenopathy or pleural effusion. In late stages of HIV infection, a primary tuberculosis – like pattern, with diffuse interstitial or military infiltrates, little or no cavitation, and intrathoracic lymphadenopathy, is more common. Overall, sputum smears may be positives less frequently among

tuberculosis patients with HIV infection than among those without; thus, the diagnosis of tuberculosis may be unusually difficult, especially in view of the variety of HIV-related pulmonary conditions mimicking tuberculosis.

Extrapulmonary tuberculosis is common among HIV infected patients. In various series, extrapulmonary tuberculosis – alone or in association with pulmonary disease-has been documented in 40-60% of all cases in HIV-co-infected individuals. The most common forms are lymphatic, disseminated, pleural, and pericardial. Mycobacteremia and meningitis are also frequent, particularly in advanced HIV disease.

The diagnosis of tuberculosis in HIV- infected patients may be difficult not only because of the increased frequency of sputum-smear negativity (upto 40% in culture-proven pulmonary cases) but also because of atypical radiographic findings, a lack of classic granuloma formation in the late stages, and a negative TST.

In general, the standard treatment regimens are equally efficacious in HIV-negative and HIV-positive patients.

Three important considerations are relevant to tuberculosis treatment in HIV-infected patients.

Immune Reconstitution inflammatory syndrome is more common among patients with advanced immunosuppression and extrapulmonary tuberculosis.

Glucocorticoids have been used for more severe reactions, although their use in this setting has not been formally evaluated in clinical trials.

Rifabutin, which has much less enzyme-inducing activity, has been recommended in place of rifampin.

CHEST X RAY IN PULMONARY TUBERCULOSIS

A normal chest film almost, although not completely, excludes pulmonary tuberculosis. There are two provisos. First, it has been shown in a number of studies that small radiological lesions are easily missed. Such observer error may be reduced by double reading by two independent observers or even by the same observer on two separate occasions. Second, it is possible for a patient to have localized post primary endobronchial tuberculosis with a positive sputum and a normal chest film.

Appearance suggestive of tuberculosis :

It is seldom possible to make a completely confident diagnosis of pulmonary tuberculosis on radiological grounds alone, as almost all the manifestations of tuberculosis can be mimicked by other diseases. The following characteristics of a chest radiograph favour the diagnosis of tuberculosis. [2]

1. Opacities mainly in the upperzone
2. Patchy or nodular opacities
3. presence of a cavity or cavities
4. Presence of calcification
5. Bilateral opacities especially if in upper zones
6. Opacities that persist after several weeks

In appropriate areas, such as North America, all these appearances can be found in histoplasmosis and most of them in coccidioidomycosis.

Pulmonary tuberculosis can mimic almost all other pulmonary diseases in much the same way that syphilis mimic most neurological diseases.

Soft confluent shadows alone suggest an exudative process and may be difficult to distinguish initially from a simple pneumonia. There may be different foci in the lungs. Linear shadows especially if they produce distortion of fissures, trachea, mediastinum or diaphragm, suggest fibrosis. Bilateral upper zone fibrotic shadows, with shrinkage of the upper lobes and elevation of the pulmonary hila, is a common picture. The presence of calcification suggests healed disease, although activity is impossible to determine solely on radiographic grounds, in many cases reactivation occurring on a back ground of an old calcified lesion. Linear and soft shadows may coexist. Tuberculosis disease is usually located in the posterior or apical segments of

the upperlobe but, exceptionally, may be restricted to the anterior segment of the upper lobe.

Cavitation results from a valvular process in a draining bronchus. Cavities in a mass of caseous material may initially have irregular wall that later become smoother and thinner as caseous material is coughed up or absorbed. A cavity may become 'blocked' and fill with purulent or caseous material, so called tuberculoma but with effective chemotherapy such lesions usually resolve satisfactorily. However, cavities may persist permanently even after effective chemotherapy and eventually be colonized by Aspergillus to produce an Aspergilloma. Tuberculous cavities may be differentiated from non tuberculosis cavities on the basis of a longer history of illness and the presence around them and in other parts of the lungs of patchy or nodular infiltrates and atelectasis. Non tuberculous cavities more often have putrid sputum, associated leucocytosis and fluid levels. CT may sometimes be used to confirm the presence of cavities and may also be useful in detecting calcification in a

suspicious lesion ; this, and the presence of satellite lesions on such tomographic studies, make the diagnosis of tuberculosis more likely.

Bronchiectasis may be suggested by elongated translucent areas in the upper zones and can be confirmed by bronchography, although this does not affect management. If such a bronchus become blocked and fills with caseous material, a so called bronchial cold abscess may form and show as a solid looking elongated dense shadow, sometimes scalloped.

Enlargement of hilar or paratracheal lymph nodes is unusual in European adults but more frequent in Asians or Africans. The lymphadenopathy and pyrexia in the presence of a positive tuberculin test may be the only manifestations of tuberculous disease. Tuberculosis limited to the lower zones of the lung is uncommon but does occur.

Radiological classification of disease extent :

For clinical and research purposes the classification of the National Tuberculosis Association of the USA has proved useful.

Minimal :

Minimal lesions include those that are of slight to moderate density but which do not contain demonstrable cavitation. They may involve a small part of one or both lungs, but the total extent, regardless of distribution, should not exceed the volume of lung on one side that occupies the space above the second chondrosternal junction and the spine of the fourth or the body of the fifth thoracic vertebra.

Moderately advanced :

Moderately advanced lesions may be present in one or both lungs, but the total extent should not exceed the following limits : disseminated lesions of slight to moderate density that may extend through out the total volume of one lung or the equivalent in both lungs ; dense and confluent lesions limited in extent to one third volume of one lung ; total diameter of cavitation, if present, must be less than 4 cm. [2]

Far advanced :

Lesions more extensive than moderately advanced.

HIV ASSOCIATED PULMONARY TUBERCULOSIS AND CHEST X RAY

As many clinical and radiological manifestations of tuberculosis depends on an intact immune system, a deficient immune system as in HIV infection alters it. The manifestations can be

1. **Progressive Primary pulmonary TB**

Usually primary tuberculosis is a self limiting infections without much complication. But in HIV patient a progressive infection is common as immunity is deficient. It can cause pleural effusion, miliary pattern, and bilateral hilar adenopathy.

2. **Post primary**

    a. Hilar and mediastinal lymphadenopathy

    b. Bilateral pleural effusion

    c. Diffuse infilterates

Lower Incidence of cavitary lesions

It is a well documented feature in many reviews. Dr. Aderaya et al[13] reported lower incidence of cavitary disease in

HIV positive individuals when compared to negative individuals in a clinical and epidemiological study.

Dr. Guilherme Freire Garcia et al[4,6] reported that in HIV patients with CD4 count < 200 the incidence of cavitation was less than 7.4% when compared to HIV patients with CD4 count > 200 – 54.5%. This study proved that the level of immuno suppression has a binding with radiological profile.

Another study by David C. Perlman[12] reported less incidence of cavitation in HIV positive individuals 50% versus 79%.

Isolated Lower zone infilterates :

HIV patients with tuberculosis is found to have more isolated lower zone infilterates in studies.

Normal chest X ray

In a study by Dr. Aderaye[13] Normal chest x ray was found in 9.2% of all the cases and was more common in HIV positive individuals.

Another study by Dr. Pepper T. Joseph[10] showed 9% patients had normal chest x ray and 58.4% patients of them were HIV positive.

Another study by Dr. Guilherme Freire Garcia et al[4] showed 14.8% normal x ray in HIV positive compared to 9% in HIV negative pulmonary TB cases.

David C. Perlman[12] showed no relation of CD4 count and normal chest x ray finding in HIV positive individuals.

HIV co-infection has got multi dimensional effect on various aspects of pulmonary tuberculosis ranging from incidence, and clinical features to investigations and management.

MATERIALS AND METHODS

The cases analysed in this study were patients who have registered under RNTCP programme in thoracic medicine department of Govt. Rajaji Hospital, Madurai after referral from various other departments.

After recording the presenting complaints, specific history of Diabetes mellitus, chronic kidney disease, immuno suppression therapy, and haematological malignancy is obtained. Patients with h/o any of the above conditions are excluded. As these condition can cause chest x ray pictures similar to HIV infection in pulmonary tuberculosis patients. A complete physical examination is done.

Patients with positive sputum AFB results whose HIV status is already checked or who are willing to check are included in the study.

After obtaining the HIV status all the patients under went chest x ray evaluation except those patients who had a recent chest x ray after diagnosis of tuberculosis.

Inclusion Criteria :

1. Pulmonary tuberculosis proved by atleast one positive sputum AFB result.
2. Presence of chest x ray taken immediately after diagnosis of tuberculosis.
3. Known HIV status.
4. Known CD4 count if HIV positive
5. Consent

Exclusion Criteria :

Any condition which can cause immuno suppression

1. Diabetes mellitus
2. Chronic kidney disease
3. Immuno suppression therapy
4. Hematological malignancy

Patients who satisfied both criteria were selected for this study.

The chest x ray features are noted down for each patients. The features studied include pleural effusion, lung collapse, cavity, alveolar opacity in upper, middle and lower zones, interstitial shadowing, hilar lymphadenopathy, pleural thickening and normal chest x ray finding.

Those patients who are found to have HIV positivity would have undergone CD4 count estimation which is available at the ART centre in Government Rajaji Hospital. The CD4 count also was noted down.

The chest x ray features were divided into two groups according to presence of atypical features. So that all the chest x rays were either having typical or atypical features.

Atypical chest x ray features includes

1. Unilateral or bilateral lower zone infiltrates without affecting respective upper zone
2. Bilateral pleural effusion
3. Normal chest x ray

4. Bilateral hilar or mediastinal lymphadenopathy
5. Interstitial shadowing

After getting all the data the following comparisons were made between the two groups.

1. Age distribution
2. Male and female ratio
3. Percentage of various chest x ray features
4. Percentage of atypical features
5. Percentage of atypical features with relation to CD4 count

RESULTS

Total number of patients studied - 60

HIV positive patients - 26

HIV negative patients - 34

Table – 1

Age Distribution

Age in years	HIV Positive	HIV Negative
< 14 years	0	0
15-29 years	6	6
30-44 years	13	12
45-59 years	7	11
> 60 years	0	5
Total	26	34

Mean age of HIV positive patients - 37.54 + 10.21

Mean age of HIV negative patients - 42.26 + 12.87

Table – 2

Sex Distribution

Sex	Pulmonary TB cases	
	HIV Positive	HIV Negative
Male	18	25
Female	8	9
Total	26	34

P value - 0.631 Not significant

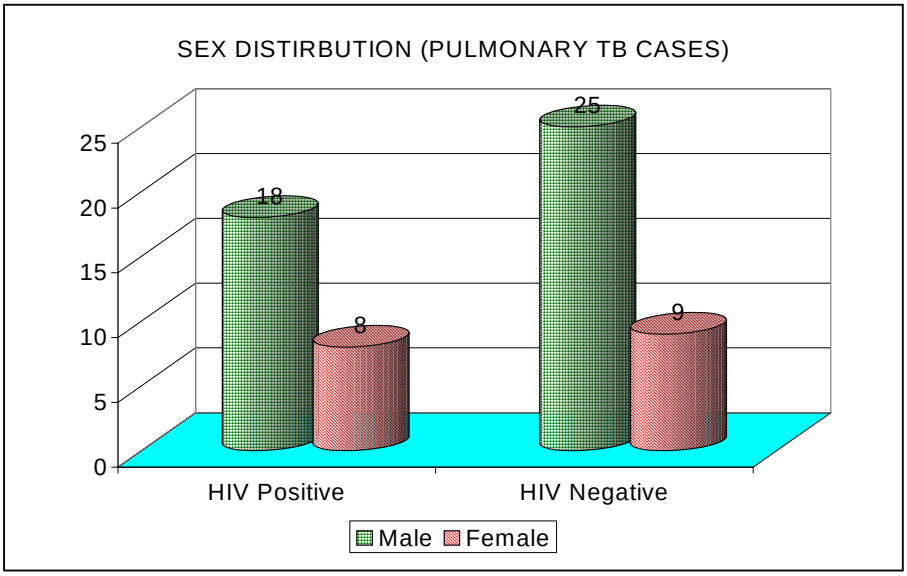


Table – 3

Various chest x ray features

	Positive	%	Negative	%	P value
Pleural effusion	5	19.2	3	8.8	0.247
Collapse	0	0	0	0	
Cavity	3	11.5	13	38.23	0.016
Upper zone	14	53.8	29	85.29	0.024
Middle zone	0	0	3	8.8	0.13
Lower zone	8	30.7	1	2.9	0.0023
Interstitial	1	3.8	0	0	0.256
Hilar adenopathy	0	0	0	0	
Pleural thickening	0	0	0	0	
Normal	7	26.9	4	11.76	0.137

HIV positive patients had significantly higher incidence of lower zone infiltrates and lower incidence of cavity and upper zone infiltrates.

Table - 4

Atypical Chest X ray

	HIV positive		HIV Negative	
	No.of patients	%	No.of patients	%
Present	16	61.5	5	14.8
Absent	10	38.5	29	85.2
Total	26		34	

P value - 0.0001 - very significant

HIV positive patients had significantly higher incidence of atypical features on chest x ray than HIV negative patients.

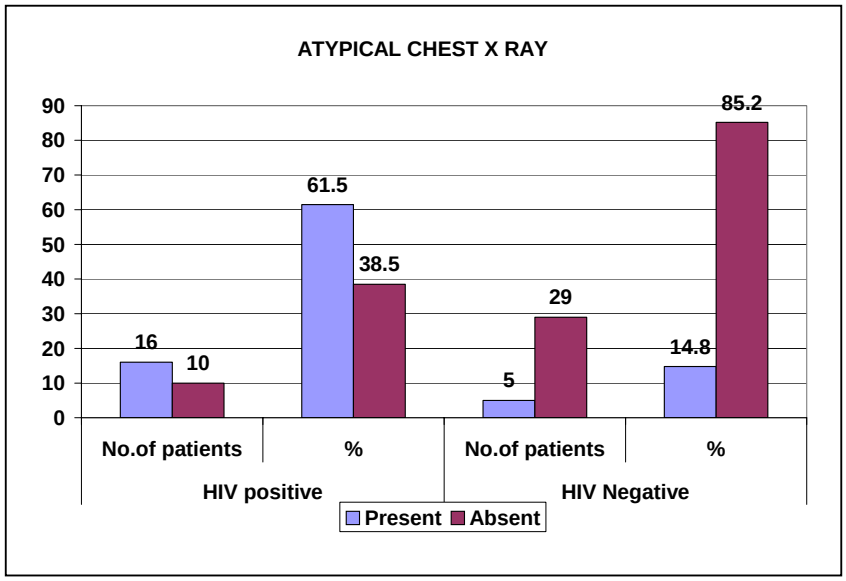
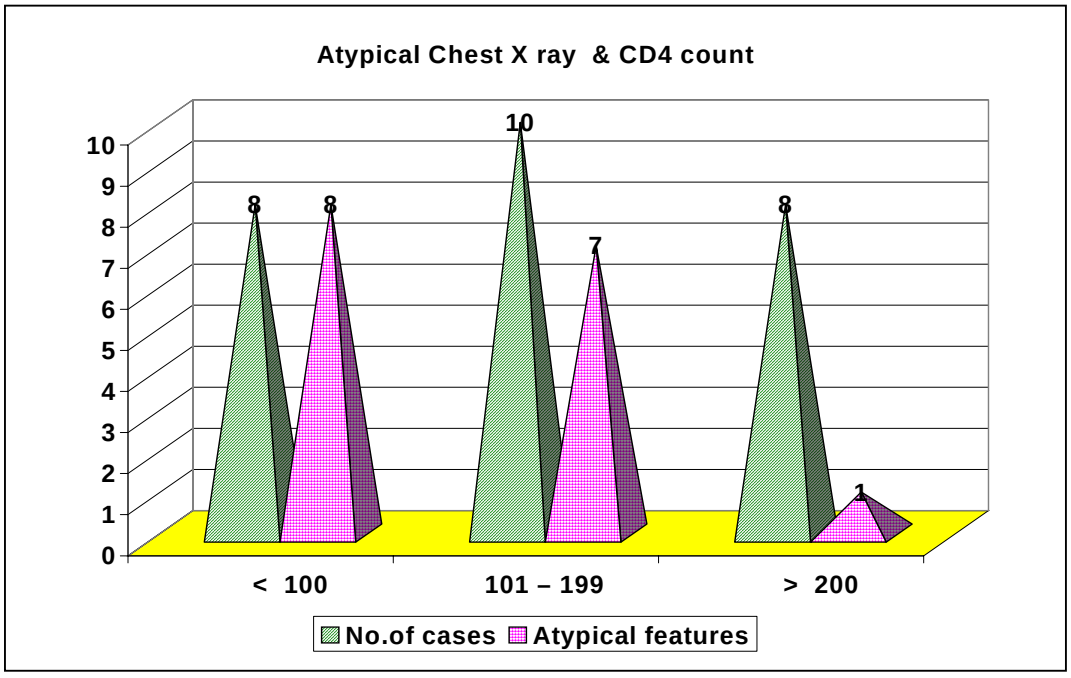


Table - 5

Atypical Chest X ray & CD4 count

CD4 count	No.of cases	Atypical features	Percentage
≤ 100	8	8	100 %
101 – 199	10	7	70%
≥ 200	8	1	12.5%

Lower CD4 count patients had higher incidence of atypical features on chest x ray.



DISCUSSION

In this study, out of the total 60 patients, 26 were HIV positive and 34 were HIV negative.

The mean age of HIV positive patients was 37 yrs and HIV negative patients was 42 years. This may indicate that the HIV positive individuals contract tuberculosis infection early. Usually tuberculosis reactivation occurs as the age progresses and immunity declines. But in HIV positive individuals immunity declines early and may cause disease at an earlier age. No patient was there in less than 14 years group. It is interesting to note that no HIV positive patient was there above the age of 60 years. This may be due to early death of HIV positive patients or due to the less risky behaviour of older persons compared to young adults.

The sex distribution of HIV positive and negative patients was equal as the p value was found to be 0.631 which indicates there was no significant difference in the two groups.

In this study there were no patient with collapse, Hilar adenopathy and pleural thickening in both groups.

Pleural effusion was found in 19.2% HIV positive patients and 8.8% in HIV negative patients. The p value of 0.247 indicates that the difference is not significant. A study by Dr. Guilherme Freire Garcia et al[4] indicated that pleural effusion was more common in HIV positive individual patients but there was no correlation between CD4 count and effusion.

Cavity was seen in 11.5% patients in HIV positive and 38.23% of patients in HIV negative individuals with a p value of 0.016 which signifies the finding. As noted before many studies found out lower incidence of cavities in HIV positive individuals. There is a correlation between CD4 count and cavity as shown in the study by Dr. Guilherme Freire Garcia et al.[4,6] As cavity formation occurs when the caseous material is couphed out. The process requires a good immune function when compared to other findings. Caseous necrosis is the final product of the granulomatous reaction caused by, lymphoid cells, epitheloid

cells and giant cells. As in HIV positive patients the cell mediated immunity is blunted more so in those having lower CD4 count, the finding of lower incidence of cavity can be explained. AL Pozniak et al[9] also showed lower incidence of cavity in HIV positive patients.

Upper zone infiltrates was found in 53.8% of HIV positive patients and 85.29% of HIV negative patients with a p value of 0.024. It is a finding of classical pulmonary tuberculosis as the bacilli can survive better in more oxygenated apical and posterior segment of upper lobe. Another reason quoted for upper lobe infilterates in pulmonary tuberculosis include the lower blood circulation and less immune activity. But in HIV positive patients as the cell mediated immunity is less the survival pressure of bacilli is less and the better blood supply of lower zones will not give a better immunity. The study by Dr. Guilherme Freire Garcia et al[4,8] showed that 64% of patients with CD4 count > 200 and none of the patients with CD4 count < 200

had upper zone infiltrates. This indicates that in pulmonary TB cases restriction of infiltrates to upper lobes is a function of cell mediated immunity.

Middle zone infiltrate were seen in none of the patients in HIV positive group and 8.8% of the HIV negative patients showed middle lobe involvement. The p value of 0.13 indicates that finding is not significant.

Lower zone infiltrates were seen in 30.7% of HIV positive patients and 2.9% in HIV negative patients with a p value of 0.0023 which showed very significant result. Diffuse infiltration were found in many studies. In the study by Dr. Guilherme Freire Garcia et al[4,7] 9.1% of patients with CD4 count > 200 and 37% of patients with CD4 count < 200 had diffuse infiltrates involving lower zones. It may be due to the inability of the immune system in HIV positive patients to contain the infection to upper lobes.

Normal chest x ray was found in 26.9% of patients with HIV and 11.76% of patients without HIV. The finding was not

significant as indicated by the p value of .137. This finding was found significant in many other studies. Dr. Aderaya et al[13,6] showed that 9.2% of patients had normal chest x ray and it was more common in HIV positive individuals with a p value of 0.05. Dr. Gream berg et al in 1994 reported that Normal chest x rays are more common when CD4 count is less than 200 (21%) when compared to CD4 count > 200 (5%).

In 2008 Pepper T. Joseph[10] reported that normal chest x ray in HIV positive patients was more likely if associated with renal failure. (p-0.048).

Atypical chest x rays were found in 21 patients. Out of that 16 patients (76%) were HIV positive and 5 patients (24%) were HIV negative. All the above studies quoted indicated higher incidence of atypical features in HIV positive individuals due to immuno suppression and decreased granuloma formation.

Among the HIV positive patients, atypical features are more common in patients with lower CD4 count. Patients with CD4 count less than 100 showed 100% presence of atypical features

and patients with CD4 count between 100 and 200 showed 70% incidence of atypical features. Patients with CD4 count > 200 had only 12.5% incidence of atypical features.

These data confirm that the atypical features are due to immuno suppression and the more the immune suppression the more the atypical features in chest x ray.

SUMMARY

- The aims of study were stated
- Literature on Tuberculous, HIV and tuberculosis co-infection, chest x ray of TB and chest x ray of HIV and TB co-infection was reviewed.
- Materials and methods of the study were stated.
- Analysis of data was done.

  Total number of patients were 60

  HIV positive patients were 26

  HIV negative patients were 34
- HIV positive patients had significantly higher incidence of lower zone infiltration.
- HIV positive patients had significantly lower incidence of cavities and upper zone infiltrates.
- Normal chest x rays are found in higher proportion of HIV positive individual but was found to be not significant.
- HIV positive patients had significantly higher incidence of atypical features on chest x ray than HIV negative patients.

- Atypical features on chest x ray correlates with CD4 count as lower CD4 count patients had higher incidence of atypical features on chest x ray.

From the discussion it was inferred that HIV co-infection is associated with higher incidence of atypical features. Atypical features found in this study included higher incidence of lower zone infiltrates and lower incidence of upper zone infiltrates and cavity. Atypical features occurred more frequently with lower CD4 count.

The diagnosis of pulmonary tuberculosis in HIV infected patients are difficult as the clinical and investigational evidences are altered especially chest radiography.

CONCLUSION

There is a significant relationship between HIV co-infection and chest radiography in pulmonary tuberculosis.

Atypical chest radiography is significantly higher in HIV co-infected patients with pulmonary tuberculosis.

Atypical chest radiographic findings are more common in patients with lower CD4 counts.

These findings emphasize the use of various investigations together with clinical features for the accurate diagnosis of pulmonary tuberculosis in patients with HIV co-infection.

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PROFORMA

Name : Date :

Age : Sex :

Address : IP/OP No. :

Complaints :

History :

Cough

Sputum

Haemoptysis

Weight loss

Fever

Examination :

Oral candidiasis

Oral hairy leukoplakia

Pulse rate

Blood pressure

CVS

RS

Abdomen

CNS

Investigations :

Blood sugar

Urea

Creatinine

Sputum AFB : CD4 count

HIV status :

CXR Features: **Right** **Left**

Pleural effusion

Lung collapse

Cavity

Alveolar opacity → Upper zone
Alveolar opacity → Middle zone
Alveolar opacity → Lower zone

Interstitial shadowing

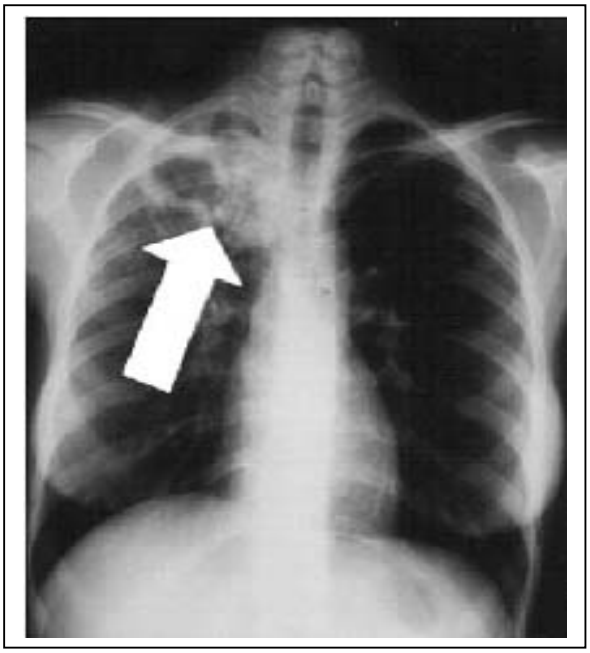
Hilar lymphadenopathy

Pleural thickening

Normal chest x ray.

Atypical chest x ray finding

RIGHT UPPER LOBE CAVITY
(HIV NEGATIVE)



DIFFUSE BILATERAL DISEASE
(HIV POSTIVE)

MASTER CHART (HIV Negative patients)

S.No.	Age	Sex	Atypical CXR	Pleural effusion	Collapse	Cavity	Alveolar infiltrates			Interstitial shadowing	Hilar Adenopathy	Normal CXR
							Upper zone	Middle zone	Lower zone			
1.	44	F	-			+	+					
2.	40	M	+									+
3.	32	M	-			+	+					
4.	42	M	-				+					
5.	54	M	-	+		+	+					
6.	29	F	-				+					
7.	48	M	+									+
8.	28	F	-	+			+					
9.	45	F	-			+	+					
10.	33	M	-				+					
11.	30	M	-			+	+					
12.	18	F	-			+	+					
13.	37	M	-				+					
14.	45	M	-			+	+					
15.	37	M	-			+	+					
16.	40	M	-				+					

17.	58	M	-			+	+					
18.	65	M	-				+					
19.	15	F	-				+					
20.	46	M	-				+					
21.	51	M	-				+					
22.	60	M	-				+	+				
23.	60	M	-				+					
24.	60	M	-				+					
25.	46	F	+						+			
26.	25	M	-				+	+				
27.	54	F	+									+
28.	39	M	-				+					
29.	42	M	-				+	+				
30.	31	M	-				+					
31.	28	M	-			+	+					
32.	61	F	+									+
33.	55	M	-				+					
34.	36	M	-				+					

MASTER CHART (HIV Positive patients)

S.No.	Age	Sex	CD4 count	Atypical CXR	Pleural effusion	Collapse	Cavity	Alveolar infiltrates			Interstitial shadowing	Hilar Adenopathy	Normal CXR
								Upper zone	Middle zone	Lower zone			
1.	43	M	242	-				+					
2.	21	F	124	+									+
3.	30	M	84	+				+		+			
4.	40	M	94	+									+
5.	37	M	398	-				+					
6.	35	F	124	+	+								
7.	55	M	196	-				+					
8.	28	F	98	+									+
9.	32	M	118	+				+		+			
10.	55	F	87	+	+								
11.	29	M	136	-	+			+					+

12.	45	M	126	+									
13.	58	M	242	-				+					+
14.	47	F	178	+	+			+					
15.	35	M	116	+									
16.	28	M	246	+			+	+		+			
17.	30	M	86	+									
18.	37	M	126	-				+		+			
19.	30	F	386	-			+	+					
20.	49	M	214	-			+	+					
21.	54	M	256	-				+		+			
22.	38	M	98	+						+			
23.	32	F	79	+						+	+		
24.	33	M	264	-				+					
25.	28	F	76	+									+
26.	27	M	126	+	+					+			